Cardiothoracic Anesthesia, Respiration and Airway

Low-dose intrathecal morphine does not delay early extubation after cardiac surgery

[L'administration intrathécale d'une faible dose de morphine ne retarde pas l'extubation précoce après une intervention chirurgicale cardiaque]

Eric Jacobsohn FRCPC,* Trevor W. R. Lee FRCPC,† Ryan J. Amadeo MD,‡ Paul H. Syslak FRCPC,‡
Roland G. Debrouwere FRCPC,‡ Dean Bell FRCPC,‡ P. Alan Klock MD,§ Heidi Tymkew MHS,* Michael Avidan MBBCH,*
The University of Manitoba Health Sciences Centre Cardiac Anesthesia Group

Purpose: This study was designed to examine the efficacy of low-dose intrathecal morphine (ITM) on extubation times and pain control after cardiac surgery.

Methods: 43 patients undergoing elective cardiac surgery were enrolled in this prospective, randomized, double-blind placebo controlled trial. Patients were given a pre-induction dose of ITM ($6 \mu\text{g}\cdot\text{kg}^{-1}$ per ideal body weight in 5 mL normal saline, group ITM) or 5 mL of intrathecal normal saline (group ITS). Anesthesia was induced with thiopental ($3 \text{ mg}\cdot\text{kg}^{-1}$), sufentanil, midazolam and rocuronium. The total allowable doses of sufentanil and midazolam for the entire case were limited to $0.5 \mu\text{g}\cdot\text{kg}^{-1}$ and $0.045 \text{ mg}\cdot\text{kg}^{-1}$ respectively. Anesthesia was maintained with isoflurane before and during cardiopulmonary bypass (CPB), and with propofol after CPB. In the postanesthesia care unit, patients received nurse-administered morphine followed by patient-controlled analgesia morphine. Serial visual analogue scale pain scores, morphine use, mini-mental state examinations and pulmonary function tests were measured for 48 hr. Patient satisfaction questionnaires were completed at the time of discharge.

Results: Mean times to extubation from the application of dressings were short and did not differ between groups (ITM = 41.4 ± 33.0 min, ITS = 39.2 ± 37.1 min). During the first 24 hr postoperatively, the ITM group had improved pain control and a lower iv morphine requirement than the control group, both at rest and during deep breathing. Both forced expiratory volume in one second and forced vital capacity were improved in the ITM group. There were no differences in spinal-related side effects or in the overall complication rates. Patient satisfac-

tion was high in both groups.

Conclusion: Low-dose ITM for cardiac surgery did not delay early extubation, but it improved postoperative analgesia and pulmonary function.

Objectif: Vérifier l'efficacité d'une faible dose de morphine intrathécale (MIT) sur le temps d'extubation précoce et le contrôle de la douleur après une opération en cardiochirurgie.

Méthode : L'étude prospective, randomisée et à double insu contre placebo a été menée auprès de 43 patients de cardiochirurgie élective. Les patients ont reçu une dose de MIT avant l'induction ($6 \mu\text{g}\cdot\text{kg}^{-1}$ par poids corporel idéal dans 5 mL de solution salée, groupe MIT) ou 5 mL de solution salée intrathécale (groupe SIT). L'anesthésie a été induite avec du thiopental ($3 \text{ mg}\cdot\text{kg}^{-1}$), du sufentanil, du midazolam et du rocuronium. Les doses totales permises de sufentanil et de midazolam pour toute l'opération ont été respectivement limitées à $0,5 \mu\text{g}\cdot\text{kg}^{-1}$ et à $0,045 \text{ mg}\cdot\text{kg}^{-1}$. L'anesthésie a été maintenue avec de l'isoflurane avant et pendant la circulation extracorporelle (CEC), et avec du propofol après la CEC. À la salle de réveil, les patients ont reçu de la morphine administrée par une infirmière, puis par injection auto-contrôlée. Les séries de scores de douleur de l'échelle visuelle analogique, la consommation de morphine, les mini-examens de l'état mental et l'exploration respiratoire fonctionnelle ont été mesurés pendant 48 h. Des questionnaires sur la satisfaction des patients ont été remplis au moment du départ.

From the Departments of Anesthesiology and Surgery, Washington University School of Medicine,* St. Louis, Missouri, USA; the Departments of Anesthesia, University of Manitoba,† and Victoria Hospital,‡ Winnipeg, Manitoba, Canada; and the Departments of Anesthesiology and Surgery, University of Chicago,§ Chicago, Illinois, USA.

Address correspondence to: Dr. Eric Jacobsohn, Department of Anesthesia and Cardiothoracic Surgery, Washington University School of Medicine, 660 South Euclid Drive, Campus Box 8054, St. Louis, MO 63110, USA. Phone: 314-747-4155; E-mail: jacobsoe@msnotes.wustl.edu. Financial support for this study was provided by the Section of Critical Care Medicine Research Fund, University of Manitoba, Winnipeg, MB, Canada.

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Résultats : Le temps moyen écoulé entre l'application de pansement et l'extubation a été court et comparable d'un groupe à l'autre (MIT = $41,4 \pm 33,0$ min, SIT = $39,2 \pm 37,1$ min). Pendant les 24 premières heures après l'opération, les patients du groupe MIT ont été mieux soulagés de leurs douleurs et ont utilisé moins de morphine iv que ceux du groupe témoin, et ce, au repos et pendant la respiration profonde. Le volume expiratoire maximum par seconde et la capacité vitale forcée ont été améliorés dans le groupe MIT. Il n'y avait pas de différence intergroupe entre les complications liées à l'injection rachidienne ou les autres complications en général. La satisfaction des patients a été élevée dans les deux groupes.

Conclusion : Une faible dose de MIT ne retarde pas l'extubation précoce et améliore l'analgésie postopératoire et la fonction pulmonaire après une opération en cardiologie.

EARLY extubation has become the standard of care after cardiac surgery.¹⁻⁵ Low-dose *iv* narcotic techniques and inhalational anesthesia are the keys to early extubation. However, achieving good postoperative analgesia can make low-dose narcotic techniques challenging. Intrathecal morphine (ITM) is an effective analgesic after cardiac surgery.⁶⁻⁸ Optimal postoperative analgesia may benefit pulmonary function, enable early mobilization, and may improve patient outcome and satisfaction.⁹ Some reports suggest that ITM delays extubation, but many of these studies used high doses of ITM (> 500 μ g), in addition to moderate to high doses of intraoperative *iv* narcotics and benzodiazepines.^{6,7} Similarly, smaller doses of ITM may be ineffective, but potential confounding factors in these studies include relatively high doses of intraoperative narcotics and sedatives, which may have prolonged extubation times.⁸

We designed a prospective, randomized, double-blinded, placebo-controlled clinical study to test the hypothesis that low-dose ITM improves pain control, does not delay extubation after cardiac surgery, and provides better postoperative analgesia when compared to postoperative *iv* patient-controlled analgesia (PCA) morphine, in the setting of a low-dose opioid, volatile-based anesthetic technique.

Methods

The study was conducted at the University of Manitoba Health Sciences Center, one of two tertiary care referral facilities for the province of Manitoba. The study protocol was approved by the University of Manitoba Ethics Committee, and patients gave written informed consent before study enrollment.

Patients were considered eligible if they were less than 80 yr of age and were scheduled for elec-

tive coronary artery bypass graft (CABG) or single valve replacement surgery. Exclusion criteria included: coagulopathy (prothrombin time > 1.3 ; partial prothrombin time > 40 sec); platelet count $< 100,000$ mm^{-3} ; the current use of any antiplatelet agent other than aspirin, non-steroidal anti-inflammatory drugs or other anticoagulant drugs, including *iv* unfractionated heparin, low-molecular weight heparin, coumadin, thrombin inhibitors, or others; inherited coagulopathy (such as von Willebrand's disease or others); the administration of preoperative inotropic drugs or preoperative intra-aortic balloon pump; preoperative mechanical ventilation; re-do or combined CABG-valve procedures; preoperative left ventricular ejection fraction $< 40\%$; current clinical diagnosis of either systolic or diastolic congestive heart failure and/or signs of interstitial or alveolar edema on chest *x-ray*; preoperative forced expiratory volume in one second (FEV₁) $< 50\%$ predicted; PaCO₂ > 45 mmHg in the absence of a primary drug induced metabolic alkalosis, body mass index > 35 $\text{kg}\cdot\text{m}^{-2}$; preoperative serum creatinine > 160 $\mu\text{mol}\cdot\text{L}^{-1}$; inability to use PCA; known opioid/benzodiazepine tolerance or addiction; known or anticipated difficult airway; current use of clonidine or steroids (for their possible confounding effects on postoperative analgesia); and any known contraindication to spinal anesthetic administration (increased intracranial pressure, sepsis, or local infection at the puncture site).

On the operative day, all patients received their usual cardiac medications as well as oral diazepam 0.1 $\text{mg}\cdot\text{kg}^{-1}$ of ideal body weight 90 min preoperatively. Ideal body weight for all body frame sizes was calculated according to the following formula: for men, weight = $51.65 \text{ kg} + [1.85 \times (\text{height} - 60 \text{ inches})]$; for women, weight = $48.67 \text{ kg} + [1.65 \times (\text{height} - 60 \text{ inches})]$, where weight is measured in kg, and height is measured in inches.¹⁰ A peripheral arterial cannula was inserted in all patients. Immediately prior to induction of anesthesia, patients were randomized into two groups. The control group (group ITS = intrathecal saline) received an intrathecal injection of 5 mL of preservative-free normal saline. The treatment group (group ITM = intrathecal morphine) received an intrathecal injection of 6 $\mu\text{g}\cdot\text{kg}^{-1}$ per ideal body weight of preservative free morphine diluted with normal saline to a final volume of 5 mL. In both groups, the pre-induction lumbar puncture was performed in the right lateral decubitus position at the L3-4 or L4-5 lumbar interspace with a 25-gauge pencil point needle. The attending anesthesiologist performing the lumbar puncture and intrathecal injection was experienced in the technique, and was also blinded

to study group assignment. When clear spinal fluid was obtained, 5 mL of study drug were injected. In the event of a bloody tap, the surgery was delayed for 24 hr. Full heparinization for cardiopulmonary bypass (CPB) was delayed for 45 min following all lumbar punctures. All staff providing subsequent care in the operating room, recovery room, and stepdown unit (SDU) remained blinded to group assignment. The patient was returned to the supine position and general anesthesia was induced. A standardized *iv* anesthetic induction was used, and included midazolam $0.015 \text{ mg}\cdot\text{kg}^{-1}$, sufentanil $0.25 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$, thiopental 2 to $3 \text{ mg}\cdot\text{kg}^{-1}$ and rocuronium $0.75 \text{ mg}\cdot\text{kg}^{-1}$. An endotracheal tube was placed and anesthesia was maintained using isoflurane titrated to an end-tidal concentration of 0.7 to 2%. Additional rocuronium was given as required, using a nerve stimulator placed over the facial nerve for drug titration. A total of $0.5 \text{ }\mu\text{g}\cdot\text{kg}^{-1}$ of sufentanil and $0.045 \text{ mg}\cdot\text{kg}^{-1}$ midazolam were administered for the entire case, with none being given after separation from CPB. A right internal jugular central venous catheter and a urinary catheter were placed after induction of anesthesia. Transesophageal echocardiography or a pulmonary artery catheter was used at the discretion of the attending anesthesiologist. Mean arterial pressure and heart rate were kept within 20% of the patient's preoperative physiological range using *iv* phenylephrine, nitroglycerine and esmolol as required. All patients were ventilated with 100% oxygen using tidal volumes of 8 to $10 \text{ mL}\cdot\text{kg}^{-1}$ with the respiratory rate adjusted to maintain an alpha stat PaCO_2 of 35 to 40 mmHg.

Standard CPB with hollow fibre membrane oxygenator was employed in all patients consisting of a 1 L crystalloid micro-prime (minimal circuit and line prime), and 12.5 g of mannitol. No steroids were given. Non-pulsatile flow was maintained at 2.2 to $2.5 \text{ L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ during CPB. Patients were not actively cooled, and core body temperature was allowed to drift to no less than 34.5°C . While on CPB, anesthesia was maintained with a minimum concentration of 1% isoflurane at all times. Phenylephrine was used as required to maintain a mean perfusion pressure of 50 to 80 mmHg. Separation from CPB was facilitated with inotropic or vasoactive drugs as deemed necessary by the attending anesthesiologist.

After separation from CPB, isoflurane was discontinued and anesthesia was maintained with propofol at 4 to $6 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$. At the end of the surgical procedure, muscle relaxation was reversed with neostigmine $0.04 \text{ mg}\cdot\text{kg}^{-1}$ and glycopyrrolate $0.008 \text{ mg}\cdot\text{kg}^{-1}$. Any non-anion gap metabolic acidosis was corrected with sodium bicarbonate administration. After the appli-

cation of surgical dressings, benzodiazepines were reversed with 0.3 mg of *iv* flumazenil.

All patients were transferred to the postanesthesia care unit (PACU) for standard postoperative care according to local institutional protocols (Appendix). Patients could be extubated in the operating room or the PACU when the following criteria were met: alert and cooperative, no focal neurologic signs, full reversal from neuromuscular blockade, tympanic temperature $> 35.5^\circ\text{C}$, adequate oxygenation and ventilation ($\text{PaO}_2 > 80 \text{ mmHg}$ on $\text{FiO}_2 < 0.5$, respiratory rate $> 10\cdot\text{min}^{-1}$ and $< 30\cdot\text{min}^{-1}$, $\text{PaCO}_2 < 55 \text{ mmHg}$), hemodynamically stable (heart rate $< 120\cdot\text{min}^{-1}$, mean arterial pressure $> 65 \text{ mmHg}$, stable cardiac rhythm), chest tube losses within acceptable limits ($< 1.5 \text{ mL}\cdot\text{kg}^{-1}$ per 30 min or $< 3 \text{ mL}\cdot\text{kg}^{-1}$ during the first hour postoperatively), acceptable acid base status ($\text{pH} > 7.27$ in absence of an unexplained metabolic acidosis), and adequate pain control for the sternotomy (visual analogue score < 5). Prior to allowing use of the PCA, *iv* morphine in 2 mg aliquots were administered by the PACU nurse, as required, to achieve a visual analogue scale (VAS) score < 5 . PCA with morphine was started in the PACU and continued for 48 hr (1.5 mg per dose, lockout 5 min). Antiemetics (metoclopramide, then dimenhydrinate) were administered as needed. Diphenhydramine (12.5 mg) was given for pruritis. Hypertension in the PACU was treated with nitroglycerine, followed by either nifedipine or labetalol as deemed appropriate by the attending anesthesiologist. From the PACU, patients were transferred to a low-intensity SDU. If indicated, patients could also be transferred to the surgical intensive care from the operating room or the PACU (for criteria, see Appendix). The SDU had no facilities for *iv* vasodilators, vasopressors, inotropes, mechanical ventilation, pulmonary artery catheters, and had a maximum nurse to patient ratio of 1:2. Central venous pressure and arterial line monitoring could be used. Patients were mobilized during the day of surgery, a liquid diet was started as early as the evening of surgery, and chest tubes and invasive lines were removed as soon as possible.

Outcome variables were defined prior to the data analysis. Time to extubation was defined as the time, in minutes, from surgical dressing application to extubation. Postoperative analgesia was evaluated using VAS pain scores at rest and with deep breathing, and by comparing cumulative postoperative morphine requirements. These were measured after extubation (time 0), and at 1, 3, 6, 12, 24 and 48 hr postoperatively. Serial pulmonary function tests [FEV_1 and forced volume capacity (FVC)] were measured using

a bedside spirometer (Welch Allyn), in the sitting position. Serial arterial blood gases were taken, and serial chest *x-rays* were assessed by a blinded radiologist for atelectasis, using an established scoring system.¹¹

In addition, serial Folstein mini-mental state examinations (MMSE) were administered to the patients.¹² Upon discharge from hospital, patients completed a previously validated patient satisfaction questionnaire that was adapted for cardiac surgery.^{13,14} This questionnaire examined analgesic satisfaction and overall satisfaction with the hospital care received.

Complications possibly related to lumbar puncture and ITM administration were recorded. These included nausea, vomiting, pruritis, headache, urinary retention, and new neurological findings. A standard questionnaire for intraoperative awareness was administered to all patients on the second postoperative day. The incidence of any other postoperative complications was recorded.

Statistics

All parameters to be included in the statistical analyses were determined prior to commencing the study. The main outcomes were time to extubation, analgesia requirements, pain scores, mental status and pulmonary function in the two groups. Power calculations were done for time to extubation and analgesia requirements. Based upon an audit of patients undergoing fast-track cardiac surgery at our institution, we observed the mean time to extubation in the PACU is 45 min (SD = 30 min). Including 20 patients in each group would provide sufficient power (87%) to detect a mean prolongation in the time to extubation of 30 min ($P < 0.05$). The mean postoperative morphine requirements in the 24 hr following fast-track cardiac surgery at our institution based upon orders of up to 4 mg·hr⁻¹ as required was 42 mg (SD = 11 mg). Including 20 patients in each group would provide sufficient power (89%) to detect a 10 mg decrease in the postoperative morphine requirements in the group that received ITM ($P < 0.05$). The power calculations were done using R. Lenth's power calculation software from the University of Iowa (www.stat.uiowa.edu/~rlenth/Power/).

Statistical analysis was performed by the University of Manitoba Department of Biostatistics utilizing SPSS (SPSS, Chicago, IL, USA). Student's *t* test (two-tailed) was used to assess the difference between the means in the two groups. Wilcoxon rank sum and Chi-square analysis were performed on non-parametric data. Repeated measures of ANOVA were used for comparisons between the groups over time, followed by least square means pair wise comparison. A *P* value of < 0.05 was considered significant.

Results

The intrathecal space was identified successfully in all patients on the first attempt. No bloody taps occurred.

Demographics

During the 4 ½ month study period, there were 164 cardiac surgery patients. The majority of these were screened and 43 patients were enrolled (Table I). There were no significant differences between the groups.

Operating room data

Both groups received similar anesthetic and surgical management (Table II). The length of time on CPB was longer in the ITM group ($P = 0.05$). Surgical and operating room times were not different between groups.

PACU

There were no differences in PACU treatments administered, and all patients were transferred from PACU to the SDU. No patient required postoperative admission to the intensive care unit.

TABLE I Patient characteristics

	Group ITS (<i>n</i> = 21)	Group ITM (<i>n</i> = 22)
<i>Preoperative characteristics</i>		
Age (yr)	64 ± 7	62 ± 11
Male	19	18
Female	2	4
Body mass index (kg·m ⁻²)	29 ± 5	28 ± 4
Height (m)	1.69 ± 0.08	1.70 ± 0.09
Weight (kg)	81 ± 13	82 ± 14
ASA score	2 ± 2	2 ± 3
Ejection fraction (%)	63 ± 12	59 ± 15
Smoking (pack yr)	32 ± 20	29 ± 23
Previous myocardial infarction	7	8
Pacemaker	1	0
Diabetes	6	8
Hypertension	10	9
Hypercholesterolemia	14	11
Stroke	0	1
<i>Preoperative medications</i>		
Nitrates	16	15
Calcium channel blockers	7	9
β-Adrenergic blockers	11	15
Oral hypoglycemic agents	5	6
Acetylsalicylic acid	15	16
Lipid lowering drugs	11	12
Furosemide	1	1
Amiodarone	1	0
Quinidine	1	0

ITS = intrathecal normal saline; ITM = intrathecal morphine. Results are expressed as the mean ± SD or the number of patients. There were no differences between groups.

TABLE II Intraoperative data

	Group ITS (<i>n</i> = 21)	Group ITM (<i>n</i> = 22)
<i>Pre-CPB</i>		
Transesophageal echocardiography used	21	22
Pulmonary artery catheter used	3	3
Mean end-tidal isoflurane (%)	0.9 ± 0.2	0.9 ± 0.2
Nitroglycerin (µg)	114 ± 289	167 ± 359
Neosynephrine (µg)	168 ± 357	152 ± 284
Ephedrine (mg)	9.5 ± 9.1	5.7 ± 9.5
Esmolol (mg)	14 ± 37	2 ± 13
<i>On-CPB</i>		
Patients having valve surgery (<i>n</i>)	1	3
Patients having CABG surgery (<i>n</i>)	20	19
Patients having LIMA graft (<i>n</i>)	17	18
Patients having RIMA graft (<i>n</i>)	4	5
Number saphenous vein grafts/patient	1.9 ± 0.2	1.9 ± 0.3
Mean CPB time (min)	54 ± 23*	72 ± 26*
Median CPB time (min) and interquartile range	47 (26-76)†‡	6 (45-78)†
Cross-clamp time (min)	33 ± 17	42 ± 18
Lowest core temperature (0°C)	35.3 ± 0.8	35.3 ± 0.6
Lowest hematocrit	0.258 ± 0.031	0.327 ± 0.161
Lowest ACT (seconds)	670 ± 79	632 ± 119
Total heparin (1,000 U)	39 ± 8	40 ± 10
Total cardioplegia solution (mL)	280 ± 127	449 ± 395
Mean "inspired" isoflurane	1.3 ± 0.31	1.3 ± 0.37
Countershocks after cross-clamp removal (<i>n</i>)	1.2 ± 1.1	0.8 ± 1.5
<i>Post-CPB</i>		
Inotrope required for separation from CPB (<i>n</i>)	2	2
Inotrope/vasopressor dependent at completion of surgery (<i>n</i>)	0	0
Nitroglycerine (µg)	127 ± 186	286 ± 699
Phenyephine (µg)	44.7 ± 79.7	32.6 ± 90
Protamine (mg)	321.6 ± 43.1	307.3 ± 56.5
Pacemaker dependent at end of surgery	2	1
Total urine for case (mL)	460.3 ± 180	558.5 ± 217.7
Surgical time (min)	169 ± 60	183 ± 38
Surgery time (min)	202 ± 54	228 ± 44
Pulmonary artery catheter removed at completion of case	3	3

Results are expressed as the mean ± SD or the number of patients. ITS = intrathecal normal saline group; ITM = intrathecal morphine group; CPB = cardiopulmonary bypass; CABG = coronary artery bypass graft; LIMA = left internal mammary artery; RIMA = right internal mammary artery. **P* = 0.05; †*P* < 0.001 between groups.

Time to extubation

The mean time to extubation was similar in both groups (Table III). All patients were spontaneously ventilating on a T-piece at the end of the operation, and only one patient per group required mechanical ventilation while in the PACU. All patients were extubated in the PACU.

Analgesia

There were significant differences in analgesic requirements between the two groups (Figures 1A-D). The number of PCA demands was greater in the ITS group; this started at four hours postoperatively and continued to 12 hr (Figure 1A). Similarly, the ITS

group had a higher requirement for morphine (Figure 1B). The VAS pain scores for chest pain at rest and with deep breathing showed that the ITM group had lower pain scores. These differences began at two hours and continued until four hours (Figures 1C, 1D).

MMSE

In both groups, MMSE scores were high during their PACU stay, but scores in the ITM group were significantly higher at four hours (Figure 2).

Pulmonary function and blood gas analysis

The ITM group had significantly better postoperative pulmonary function as measured with bedside spi-

TABLE III Postoperative data

	Group ITS (n = 21)	Group ITM (n = 22)
<i>PACU</i>		
Mean time to extubation (min)	39.2 ± 37.1	41.4 ± 33.0
Median time to extubation (min), interquartile range	24, (30-120)	35, (24-113)
Patients (n) extubated in time period:		
0-15 min	5	4
15-30	8	4
30-45	2	5
45-60	1	4
60-90	2	3
> 90	3	2
Patients requiring a mechanical ventilator in PACU* (n)	1	1
Mean time to first <i>iv</i> morphine dose (min)	13.4 ± 30.1	27.4 ± 46.3
PACU discharge criteria met (min)	125.5 ± 229.2	82.0 ± 129.7
Patients requiring reintubation (n)	0	0
Patients with intraoperative awareness (n)	0	0
<i>SDU and ward</i>		
Episodes of nausea/patient in first 48 postoperative hours (n)	0.7 ± 0.7	0.7 ± 0.9
Episodes of vomiting/patient in first 48 postoperative hours (n)	0	0
Episodes of pruritis/patient in first 48 postoperative hours (n)	0.4 ± 0.8	1.0 ± 1.2
Episodes patients with a headache requiring treatment (n)	2	1
Patients with a PDPH (n)	0	0
Patients with new neurological findings (n)	0	0
Patients with urinary retention after catheter removed (n)	0	0
Patients with atrial fibrillation or flutter requiring treatment (n)	5	5
Patients requiring admission to ICU from the SDU or ward (n)	0	0
Analgesic satisfaction (0-10)	8.3 ± 1.9	8.4 ± 1.6
Overall hospital satisfaction (0-10)	8.5 ± 1.0	8.1 ± 1.0
Mean hospital length of stay (days)	5.8 ± 1.9	5.3 ± 1.5

*Patients breathing on a T-piece to wall oxygen are considered non-ventilated. ITS = intrathecal normal saline group. ITM = intrathecal morphine group. PACU = postanesthesia care unit; PDPH = postdural puncture headache. ICU = intensive care unit; SDU = stepdown unit. There were no differences between the groups.

rometry. Both groups exhibited marked decreases in FEV₁, but the decline was not as pronounced in the ITM group. This effect started at two hours and persisted up to 24 hr postoperatively (Figure 3A). Similarly, the ITM group also had higher percent-predicted FVC measurements throughout the first 24 hr (Figure 3B). There were no differences in the PaCO₂, PaO₂ or atelectasis scores (Figures 3C, 3D).

Patient satisfaction

Both groups had high scores for overall patient satisfaction and analgesia (Table III). There were no differences between groups.

Side effects and complications

There were no differences in the incidence of nausea, vomiting, or pruritis (Table III). The incidence of postoperative headache was low, and no patient required treatment for postdural puncture headache. There were no differences between groups in post-

operative complications, including atrial fibrillation, atrial flutter, premature ventricular complex, sinus tachycardia, brady arrhythmias requiring pacing, respiratory complications, urinary retention, pleural effusions or poor diabetic control.

Discussion

Regional anesthesia for cardiac surgery is gaining in popularity, although it remains controversial.⁵ We showed low-dose ITM analgesia (6 µg·kg⁻¹ of ideal body weight) improves postoperative spirometry, without delaying extubation, and provides adequate postoperative analgesia with lower *iv* morphine use, when compared to control patients receiving general anesthesia alone.

Previously it has not been well established that low-dose ITM improves spirometry after cardiac surgery, although the effect has been shown with high-dose ITM.¹⁶ In the present investigation, the use of ITM resulted in improved postoperative pulmonary func-

FIGURE 1 A-D) Postoperative pain control: 1A) Total patient controlled analgesia demands; 1B) Total morphine required (mg); 1C) Visual analogue pain scores for chest pain at rest; 1D) Visual analogue pain scores for chest pain with deep breathing. † $P < 0.05$, ‡ $P < 0.01$, ¥ $P < 0.005$, * $P < 0.001$, between groups.

tion as measured by bedside spirometry. The FEV_1 and FVC decreased in both groups, but there was a smaller decline in FEV_1 and FVC in the ITM group in the first 24 hr. The improved spirometry was likely related to better analgesia in the ITM group, as determined by decreased postoperative *iv* morphine requirements. However, there were no significant differences in serial PaO_2 , A-a gradient measurements, or atelectasis scores between groups. Whether the improvement in spirometry with ITM could have clinical implications for postoperative pulmonary complications, including chest infection, could not be demonstrated in this small sample size study. A similar study in a larger population may better address that issue.

As shown in a recent meta-analysis by Liu *et al.*, previous studies using high-dose ITM resulted in extubation times that were generally long (10.4 hr for intrathecal groups *vs* 10.9 hr for general anesthesia groups).¹⁷ This analysis also demonstrated that general anesthesia combined with low-dose ITM (< 500 μ g or < 7 μ g·kg⁻¹) resulted in a modest decrease in systemic morphine use, and slightly faster extubation times. However, extubation times in this subgroup were 7.1 hr for intrathecal *vs* 9.3 hr for general anesthesia groups. In comparison, extubation times in our study were short, but not significantly different (41.4 ± 33.0 min *vs* 39.2 ± 37.1 min for ITM and ITS groups, respectively). In the small number of patients studied, early extubation was practical and without untoward effect following low-dose ITM. No patient required reintubation, and no patient was admitted to the intensive care unit.

FIGURE 2 MMSE = postoperative mini mental state evaluation scores (percent of preoperative score). † $P < 0.05$ between groups.

Although it has been well-established that ITM provides improved analgesia after cardiac surgery, this effect has not been extensively demonstrated with low-dose ITM analgesia.^{8,18-20} In the present study, we have shown that low-dose ITM allows for early extubation, while also providing improved pain control. A standardized anesthetic technique minimized the postoperative confounding variables for extubation time and analgesia, and also ensured that the patients were awake and cooperative soon after surgery; the patients were able to accurately participate in postoperative measurements of pain, mini-mental state and respiratory function. The ITM dose and *iv* sufentanil dose (0.5 – 0.75 μ g·kg⁻¹ sufentanil) were comparatively low and therefore minimized postoperative drowsiness and side effects. Similarly, the low doses of fixed agents used during maintenance of anesthesia were selected to improve the probability of early extubation. The ITM group required less total morphine, made fewer PCA demands, and had lower VAS pain scores at rest, and more importantly, with deep breathing. The analgesic effect was present on emergence and persisted during the first day. Considering pharmacokinetics of ITM, this time course of the analgesia was expected.²¹

The classic side effects of pruritis, nausea, vomiting, urinary retention and ventilatory depression are dose-related, with doses in excess of 0.5 mg having a higher incidence.²² As expected, with the low-dose of ITM studied, the adverse side effects related to ITM were minimal. Patients were satisfied with their analgesia and overall hospital care. Satisfaction scores for our study were high, but not different between groups.

FIGURE 3 A-D) Measured forces expiratory volume in one second (FEV₁)/predicted FEV₁; 3A) Measured/Predicted FEV₁; 3B) Measured/predicted FVC; 3C) PaCO₂ (mmHg) and A-aDO₂ (mmHg); 3D) Atelectasis scores. Results are graphically presented as a proportion of 1.0. †*P* < 0.05, ‡*P* < 0.01, ¥*P* < 0.005, **P* < 0.001, between groups.

The risk of epidural or subarachnoid hematoma with lumbar puncture before cardiac surgery remains a concern. However, the most recent analysis estimates the risk of spinal hematoma in patients receiving spinal blockade for cardiac surgery is in the range of 1:220,000 to 1:3,600, with 95% confidence.²³ In addition to excluding patients with a coagulopathy (other than currently being on aspirin), in order to minimize theoretical risks, we used a 25-gauge spinal needle in the midline approach, allowed lumbar puncture attempts only by a person experienced with the technique, and delayed heparin administration for 45 min after performing the spinal. We believe that the potential benefits of improved spirometry, early extubation, and excellent analgesia outweigh the risks of lumbar puncture in this select group of patients.

This investigation did not evaluate the effects of ITM on stress hormones during cardiac surgery. However, a previous study by Hall *et al.* did show a partial attenuation of the stress response after cardiac surgery using ITM combined with general anesthesia.²⁴ More recently, Lee *et al.* also showed a

significant blunting of the stress hormone response to cardiac surgery, as well as a favourable change in cardiac metabolism, in patients receiving high-dose intrathecal bupivacaine combined with general anesthesia for cardiac surgery.²⁵ Future studies involving larger sample sizes should examine the combined use of high-dose intrathecal bupivacaine and low-dose ITM on the stress-response to cardiac surgery and postoperative outcomes.

In conclusion, the use of low-dose ITM in patients having cardiac surgery was associated with improved postoperative spirometry, improved postoperative analgesia when compared to PCA morphine, and no delay time to extubation. The technique was not associated with increase in adverse events and the patient satisfaction was high. When combined with general anesthesia, low-dose ITM offers an alternative anesthetic technique, which appears to have some benefits over general anesthesia alone for cardiac surgery.

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APPENDIX

ICU admission criteria

There were no operation-specific criteria for admission to the intensive care unit (ICU). The decision to admit to ICU was based on physiological aberrations present at the end of the operation or that developed in the postanesthesia care unit. These included:

- 1) Hemodynamic instability or anticipated hemodynamic instability requiring vasopressor, inotrope or intra-aortic balloon-pump counter pulsation;
- 2) Arrhythmias requiring ongoing treatment;
- 3) Inability to extubate within the first four hours;
- 4) Coagulopathy requiring ongoing treatment;
- 5) Patients with renal failure requiring dialysis or renal impairment ($\text{Cr} > 160 \mu\text{mol}\cdot\text{L}^{-1}$) needing frequent electrolyte and possibly pulmonary artery catheter monitoring;
- 6) Need for a pulmonary artery catheter;
- 7) Morbid obesity;
- 8) Obstructive sleep apnea